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=> index bioscience

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE, AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS, CEABA-VTB, CIN, CONFSCI, CROPB, CROPII, DDFB, DDFUI, DGENE, DISSABS, DRUGB, DRUGMONOG2, DRUGU, EMBAL, EMBASE, ...' ENTERED AT 09:27:57 ON 09 OCT 2008

69 FILES IN THE FILE LIST IN STNINDEX

=> ANALGESIA? OR NOCICEPTION OR PAIN OR (CHRONIC PAIN)

28374 FILE ADISCTI  
2403 FILE ADISINSIGHT  
11403 FILE ADISNEWS  
3206 FILE AGRICOLA  
125 FILE ANABSTR  
385 FILE ANTE  
44 FILE AQUALINE  
412 FILE AQUASCI  
2167 FILE BIOENG  
200625 FILE BIOSIS  
2129 FILE BIOTECHABS  
2129 FILE BIOTECHDS  
8286 FILE BIOTECHNO  
16455 FILE CABA  
76645 FILE CAPLUS  
113 FILE CEABA-VTB  
2937 FILE CIN  
4664 FILE CONFSCI  
2 FILE CROPB  
92 FILE CROPII  
6586 FILE DDFB  
55789 FILE DDFUI  
164159 FILE DGENE  
9671 FILE DISSABS  
6586 FILE DRUGB  
265 FILE DRUGMONOG2  
81664 FILE DRUGU  
3458 FILE EMBAL  
380219 FILE EMBASE  
50477 FILE EMBIOBASE  
204 FILE FOMAD  
108 FILE FOREGE  
696 FILE FROSTI  
285 FILE FSTA  
34 FILES SEARCHED...  
31231 FILE GENBANK  
2314 FILE HEALSAFE  
18214 FILE IHPAT  
2902 FILE IMSDRUGNEWS  
12587 FILE IMSPRODUCT  
1717 FILE IMSRESEARCH  
258 FILE KOSMET  
21238 FILE LIFESCI  
344075 FILE MEDLINE  
1848 FILE NTIS  
202 FILE NUTRACEUT  
87 FILE OCEAN  
127815 FILE PASCAL  
16727 FILE PCTGEN  
2223 FILE PHAR  
2684 FILE PHARMAMI

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43 FILE PHIC  
 9083 FILE PHIN  
 114839 FILE PROMT  
 11609 FILE PROISDDR  
 45 FILE RDISCLOSURE  
 225735 FILE SCISEARCH  
 36 FILE SYNTHLINE  
 97153 FILE TOXCENTER  
 42270 FILE USGENE  
 100315 FILE USPATFILL  
 7726 FILE USPATOLD  
 15229 FILE USPAT2  
 79 FILE VETB  
 2277 FILE VETU  
 76 FILE WATER  
 40314 FILE WPIDS  
 1442 FILE WPIFV  
 40314 FILE WPINDEX

68 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STNINDEX

L1 QUE ANALGESIA? OR NOCICEPTION OR PAIN OR (CHRONIC PAIN)

=> (inhibitor or downmodulator or (slow down)) (5a) ((glutamine synthetase) or (glutamate dehydrogenase) or (pyruvate carboxylase) or (glutamine cycle) or ((glial cell) (5a)(TCA cycle)))

75 FILE AGRICOLA  
 2 FILE ANABSTR  
 2 FILE AQUALINE  
 30 FILE AQUASCI  
 49 FILE BIOENG  
 524 FILE BIOSIS  
 42 FILE BIOTECHABS  
 42 FILE BIOTECHDS  
 12 FILES SEARCHED...  
 87 FILE BIOTECHNO  
 154 FILE CABA  
 598 FILE CAPLUS  
 17 FILE CEABA-VTB  
 16 FILES SEARCHED...  
 3 FILE CIN  
 4 FILE CONFSCI  
 2 FILE CROPB  
 26 FILE CROPU  
 5 FILE DDFB  
 21 FILE DDFU  
 104 FILE DGENE  
 25 FILE DISSABS  
 5 FILE DRUGB  
 26 FILES SEARCHED...  
 26 FILE DRUGU  
 1 FILE EMBAL  
 212 FILE EMBASE  
 143 FILE ESBIOBASE  
 30 FILES SEARCHED...  
 3 FILE FROSTI  
 1 FILE FSTA  
 717 FILE GENBANK  
 50 FILE IHIPAT

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1 FILE IMSRESEARCH  
 174 FILE LIFESCI  
 236 FILE MEDLINE  
 1 FILE NTIS  
 2 FILE OCEAN  
 134 FILE PASCAL  
 47 FILES SEARCHED...  
 3 FILE PHIN  
 4 FILE PROMT  
 7 FILE PROUSDDR  
 1 FILE RIDISCLOSURE  
 255 FILE SCISEARCH  
 194 FILE TOXCENTER  
 22 FILE USGENE  
 749 FILE USPATFULL  
 61 FILES SEARCHED...  
 162 FILE USPAT2  
 2 FILE WATER  
 57 FILE WPIDS  
 1 FILE WPIFV  
 57 FILE WPINDEX  
 48 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STNINDEX  
 L2 QUE (INHIBITOR OR DOWNMODULATOR OR (SLOW DOWN)) (5A) ((GLUTAMINE SYNTHETAS  
 E) OR (GLUTAMATE DEHYDROGENASE) OR (PYRUVATE CARBOXYLASE) OR (GLUTAMIN  
 E CYCLE) OR ((GLIAL CELL) (5A)(TCA CYCLE)))

=> (((peripheral) (5a) nervous system)) (5a) (inflammation site)

16 FILES SEARCHED...  
 30 FILES SEARCHED...  
 1 FILE IFIPAT  
 47 FILES SEARCHED...  
 2 FILE USPATFULL  
 2 FILE USPAT2  
 66 FILES SEARCHED...

3 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STNINDEX

L3 QUE (((PERIPHERAL) (5A) NERVOUS SYSTEM)) (5A) (INFLAMMATION SITE)

=> administer? or give? or appl? or administer or give or apply

49180 FILE ADISCTI  
 8274 FILE ADISINSIGHT  
 23300 FILE ADISNEWS  
 243421 FILE AGRICOLA  
 142289 FILE ANABSTR  
 86254 FILE ANTE  
 80343 FILE AQUALINE  
 189175 FILE AQUASCI  
 143636 FILE BIOENG  
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 291856 FILE BIOTECHABS  
 291856 FILE BIOTECHDS  
 193567 FILE BIOTECHNO  
 1143502 FILE CABA  
 6195254 FILE CAPLUS  
 125095 FILE CEABA-VTB

Search Performed on 10/09/2008

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127863 FILE CIN  
17 FILES SEARCHED...  
57415 FILE CONFSCI  
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137677 FILE CROPU  
32779 FILE DDFB  
212697 FILE DDFU  
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32779 FILE DRUGB  
492 FILE DRUGMONOG2  
437166 FILE DRUGII  
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1524476 FILE EMBASE  
931985 FILE ESBIOBASE  
29165 FILE FOMAD  
4144 FILE FOREGE  
136991 FILE FROSTI  
165580 FILE FSTA  
34 FILES SEARCHED...  
4621165 FILE GENBANK  
37887 FILE HEALSAFE  
2413270 FILE IIFPAT  
8441 FILE IMSDRUGNEWS  
278 FILE IMSPRODUCT  
11812 FILE IMSRESEARCH  
14042 FILE KOSMET  
406314 FILE LIFSCI  
1652542 FILE MEDLINE  
608384 FILE NTIS  
2340 FILE NUTRACEUT  
51729 FILE OCEAN  
2020657 FILE PASCAL  
22599 FILE PCTGEN  
10006 FILE PHAR  
21044 FILE PHARMAML  
341 FILE PHIC  
119793 FILE PHIN  
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8 FILE PS  
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7267 FILE SYNTHLINE  
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2614212 FILE USPATOLD  
709148 FILE USPAT2  
3361 FILE VETB  
38139 FILE VETU  
128230 FILE WATER  
66 FILES SEARCHED...  
2919457 FILE WPIDS  
33188 FILE WPIFV  
2919457 FILE WPINDEX

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Searcher: Kailash C. Srivastava

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69 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STINDEX

L4 QUE ADMINISTER? OR GIV? OR APPL? OR ADMINISTER OR GIVE OR APPLY

=> L2 and L3

11 FILES SEARCHED...  
13 FILES SEARCHED...  
23 FILES SEARCHED...  
30 FILES SEARCHED...  
44 FILES SEARCHED...  
47 FILES SEARCHED...  
61 FILES SEARCHED...

0 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STINDEX

L5 QUE L2 AND L3

=> L2 and L4

12 FILE AGRICOLA  
3 FILE BIOENG  
55 FILE BIOSIS  
19 FILE BIOTECHABS  
19 FILE BIOTECHDS  
12 FILES SEARCHED...  
10 FILE BIOTECHNO  
28 FILE CABA  
75 FILE CAPLUS  
17 FILES SEARCHED...  
1 FILE CROPB  
13 FILE CROPU  
10 FILE DGENE  
5 FILE DISSABS  
2 FILE DRUGU  
1 FILE EMBAL  
23 FILE EMBASE  
52 FILE ESBIOBASE  
30 FILES SEARCHED...  
2 FILE FROSTI  
61 FILE GENBANK  
36 FILE IFIPAT  
1 FILE IMSRESEARCH  
20 FILE LIFESCI  
28 FILE MEDLINE  
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46 FILES SEARCHED...  
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1 FILE PHIN  
2 FILE PROMIT  
1 FILE RDISCLOSURE  
36 FILE SCISEARCH  
35 FILE TOXCENTER  
1 FILE USGENE  
749 FILE USPATTULL  
162 FILE USPAT2  
63 FILES SEARCHED...  
43 FILE WPIDS  
43 FILE WPINDEX

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34 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STNINDEX

L6 QUE L2 AND L4

=> L3 and L4

13 FILES SEARCHED...

30 FILES SEARCHED...

1 FILE IFPAT

47 FILES SEARCHED...

2 FILE USPATFULL

2 FILE USPAT2

65 FILES SEARCHED...

3 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STNINDEX

L7 QUE L3 AND L4

=> L1 and L6

1 FILE BIOSIS

11 FILES SEARCHED...

13 FILES SEARCHED...

3 FILE CAPLUS

25 FILES SEARCHED...

1 FILE EMBASE

1 FILE EMBASE

30 FILES SEARCHED...

2 FILE GENBANK

1 FILE IFPAT

1 FILE IMSRESEARCH

1 FILE LIFESCI

1 FILE MEDLINE

44 FILES SEARCHED...

47 FILES SEARCHED...

1 FILE SCISEARCH

2 FILE TOXCENTER

15 FILE USPATFULL

61 FILES SEARCHED...

4 FILE USPAT2

1 FILE WPIDS

1 FILE WPINDEX

15 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STNINDEX

L8 QUE L1 AND L6

=> L7 and L8

10 FILES SEARCHED...

12 FILES SEARCHED...

13 FILES SEARCHED...

23 FILES SEARCHED...

30 FILES SEARCHED...

42 FILES SEARCHED...

47 FILES SEARCHED...

59 FILES SEARCHED...

67 FILES SEARCHED...

0 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STNINDEX

L9 QUE L7 AND L8

L1 and L7

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12 FILES SEARCHED...

26 FILES SEARCHED...

35 FILES SEARCHED...

1 FILE IFPAT

47 FILES SEARCHED...

2 FILE USPATFULL

1 FILE USPAT2

63 FILES SEARCHED...

3 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STINDEX

L10 QUE L1 AND L7

=> d Rank

F1 2 USPATFULL

F2 1 IFPAT

F3 1 USPAT2

=> file f1, f2, f3

FILE 'USPATFULL' ENTERED AT 10:00:40 ON 09 OCT 2008

CA INDEXING COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'IFPAT' ENTERED AT 10:00:40 ON 09 OCT 2008

COPYRIGHT (C) 2008 IFI CLAIMS(R) Patent Services (IFI)

FILE 'USPAT2' ENTERED AT 10:00:40 ON 09 OCT 2008

CA INDEXING COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

=> L10

L11 4 L10

=> D L11 1-4

L11 ANSWER 1 OF 4 USPATFULL on STN

AN 2007:88980 USPATFULL

TI BIOINFORMATICAALLY DETECTABLE GROUP OF NOVEL VACCINIA REGULATORY GENES  
AND USES THEREOF

IN Bentwich, Itzhak, 65 Kfar Daniel, Kfar Daniel, ISRAEL 73125

PA ROSETTA GENOMICS, Rehovot, ISRAEL (non-U.S. corporation)

PI US 20070077553 A1 20070405

AI US 2003-605840 A1 20031030 (10)

DT Utility

FS APPLICATION

LN,CNT 126036

INCL INCLM: 435/005.000

INCLS: 435/006.000; 536/023.720; 702/020.000

NCL NCLM: 435/005.000

NCLS: 435/006.000; 536/023.720; 702/020.000

IC IPCI C12Q0001-70 [I,A]; C12Q0001-68 [I,A]; G06F0019-00 [I,A];  
G01N0033-48 [I,A]; G01N0033-50 [I,A]; C07H0021-04 [I,A];  
C07H0021-00 [I,C\*]

IPCR C12Q0001-70 [I,C]; C12Q0001-70 [I,A]; C07H0021-00 [I,C];  
C07H0021-04 [I,A]; C12Q0001-68 [I,C]; C12Q0001-68 [I,A];  
G01N0033-48 [I,C]; G01N0033-48 [I,A]; G01N0033-50 [I,C];  
G01N0033-50 [I,A]; G06F0019-00 [I,C]; G06F0019-00 [I,A]

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 2 OF 4 USPATFULL on STN

AN 2007:36283 USPATFULL

TI BIOINFORMATICAALLY DETECTABLE GROUP OF NOVEL VACCINIA REGULATORY GENES

## AND USES THEREOF

IN Bentwich, Itzhak, 65 Kfar Daniel, Kfar Daniel, ISRAEL 73125  
 PA ROSETTA GENOMICS, Rehovot, ISRAEL (non-U.S. corporation)  
 PI US 20070031823 A1 20070208  
 AI US 2003-604943 A1 20030828 (10)  
 PRAI US 2003-441241P 20030117 (60)  
 DT Utility  
 FS APPLICATION  
 LN,CNT 61464  
 INCL INCLM: 435/005.000  
 INCLS: 536/023.720; 702/020.000  
 NCL NCLM: 435/005.000  
 NCLS: 536/023.720; 702/020.000  
 IC IPCI C12Q0001-70 [I,A]; G06F0019-00 [I,A]; G01N0033-48 [I,A];  
 G01N0033-50 [I,A]; C07H0021-04 [I,A]; C07H0021-00 [I,C\*]  
 IPCR C12Q0001-70 [I,C]; C12Q0001-70 [I,A]; C07H0021-00 [I,C];  
 C07H0021-04 [I,A]; G01N0033-48 [I,C]; G01N0033-48 [I,A];  
 G01N0033-50 [I,C]; G01N0033-50 [I,A]; G06F0019-00 [I,C];  
 G06F0019-00 [I,A]

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 3 OF 4 IFPAT COPYRIGHT 2008 IFI on STN

AN 04693467 IFPAT;IFIUDB;IFICDB

TI Method of alleviating chronic pain via peripheral  
 glutaminase regulation; Administering glutaminase inhibitor to  
 a subject suffering from chronic pain at a site of  
 inflammation for therapy of chronic pain

IN Miller Kenneth E

PA Oklahoma, University of Board of Regents (61802)

PI US 7288246 B2 20071030

US 20030072746 A1 20030417

AI US 2002-245098 20020913

PRAI US 2001-318861P 20010913 (Provisional)

FI US 7288246 20071030

US 20030072746 20030417

DT Utility; Granted Patent - Utility, with Pre-Grant Publication

FS CHEMICAL

GRANTED

ED Entered STN; 2 Nov 2007

Last Updated on STN: 28 Apr 2008

CLMN 16

GI 22 Drawing Sheet(s), 22 Figure(s).

FIG. 1 is a diagrammatic representation of the effects of Glutamate and glutaminase on peripheral sensory nerve stimulation and exacerbation of pain responses.

FIG. 2 is a model regarding glutamate production in primary sensory neurons during chronic inflammation. Inflammatory mediators (lightning bolts) activate and sensitize peripheral afferent terminals. This leads to the release of glutamate (GLU) and other substances from peripheral terminals causing further sensitization (arrow). Inflammation stimulates keratinocytes to increase production of nerve growth factor (NGF). NGF is taken up and retrogradely transported to the neuronal cell body where it stimulates increased production of glutaminase (GT). Increased production of GT occurs from stabilization of GT mRNA via zeta-crystallin:quinone oxidoreductase (ZC). Increased amounts of GT are shipped to the periphery causing elevated glutamate production and release, further primary afferent sensitization, and exacerbation of nociceptive responses.

FIG. 3 are photomicrographs illustrating the effects of fixation on

glutaminase (GT) immunoreactivity (IR) in the rat dorsal root ganglia (DRG). DRG sections were processed simultaneously with a mouse monoclonal GT antibody (A, C) or a rabbit polyclonal GT antiserum (B, D). Some DRG's (A,B) were fixed with 4% paraformaldehyde and others (C,D) were fixed with 70% picric acid and 0.2% paraformaldehyde. In paraformaldehyde fixed tissue, intense GT-IR was restricted to small sized DRG neurons (long arrows) with both GT antibodies (A,B). Large to medium sized neurons (short arrows) were lightly stained (A,B). In picric acid-paraformaldehyde fixed tissue, small (long arrows) and medium to large sized neurons (short arrows) contained intense GT-IR with both GT antibodies (C,D). For FIG. 4 and the data utilized to produce FIGS. 5 and 6, picric acid-paraformaldehyde fixed tissue was used with the rabbit polyclonal GT antiserum.

FIG. 4 are photomicrographs illustrating Glutaminase (GT) immunoreactivity (IR) in rat L4 dorsal root ganglia (DRG) following 7 days of CFA inflammation in the right hindpaw. DRG sections were processed simultaneously with a rabbit polyclonal GT antiserum and photographed under identical conditions. (A) In control sections, GT-IR was light to moderate in all neuronal cell sizes, small (long arrows) and medium to large (short arrows). (B) Increased GT-IR intensity was observed in small (long arrows) and medium to large neurons (short arrows) in the left (contralateral) DRG following right hindpaw inflammation. This modest increase of GT-IR was observed in the left DRG at 3 & 10 days, also. (C) Elevated GT-IR in small (long arrows) and medium to large (short arrows) neurons occurred in the right (ipsilateral) DRG following CFA inflammation of right hindpaw. This pattern also was observed at 3 & 10 days following inflammation.

FIG. 5 is a graphic illustration of an image analysis of glutaminase (GT) immunoreactivity (IR) in L4 DRG neurons after 7 days of CFA inflammation in the right paw. Data are presented as intensity divided by the area of the cell. DRG neurons were categorized into three area size groups: (A) small 100 600  $\mu\text{m}^2$ , (B) medium 600 1200  $\mu\text{m}^2$ , (C) large  $>1200 \mu\text{m}^2$ . (A) Small sized neurons in the left DRG contained a significantly greater immunoreactive signal (\*,  $p<0.05$ ) than controls. Neurons in the right DRG were more intensely stained than left DRG or controls (\*\*,  $p<0.01$ ). (B) Medium sized neurons in the left DRG contained a significantly greater immunoreactive signal (\*,  $p<0.05$ ) than controls. Neurons in the right DRG were more intensely stained than left DRG or controls (\*\*,  $p<0.01$ ). (C) In the right DRG, large sized neurons were more intensely stained than the left DRG or controls (\*,  $p<0.05$ ).

FIG. 6 is a graphic illustration of GT enzyme activity in the L4 DRG at 7 days following CFA inflammation in the right hindpaw. GT activity from the right DRG ( $2.83 \pm 0.30$  moles/kg/hr) was elevated (\*,  $p<0.05$ ) over control values ( $2.20 \pm 0.18$  moles/kg/hr). The left (contralateral) L4 DRG ( $2.61 \pm 0.20$  moles/kg/hr) was not significantly different from controls or the right (ipsilateral) DRG.

FIG. 7 is a diagrammatic representation of the effects of inhibition of glutaminase on thermal and mechanical pain. The hindpaw responses to thermal stimulation (FIG. 7A) and pressure sensitivity (FIG. 7B) were determined for a control rat, a control rat following glutaminase inhibition with 6 diazo-5-oxo-L-norleucine (DON), a rat after CFA inflammation, and a rat after CFA inflammation and following glutaminase inhibition with DON.

FIG. 8A is a graphic representation illustrating the efficacy of DON to provide long term pain relief from pressure (mechanical stimulation). After administration of DON at day three following CFA inflammation, pain relief occurred for several days with three different doses of DON (0.1 10 Mole/25  $\mu\text{m}^2$ ).

FIG. 8B is a graphic representation representing the DON dose response for pain relief from pressure stimulation. The area under the curve for each dose was determined from Day 3 to Day 5. No differences in the amount of pain relief were determined for the doses tested (0.1 10 mu Mole/25 mu l).

FIG. 9A is a graphic representation illustrating the efficacy of DON to provide long term pain relief to heat. After administration of DON at day three following CFA inflammation, pain relief occurred for several days with three different doses of DON (0.1 10 mu Mole/25 mu l).

FIG. 9B is a graphic representation illustrating the DON dose response for pain relief from thermal stimulation. The area under the curve for each dose was determined from Day 3 to Day 5. Pain relief was most efficacious at the higher doses (1 10 mu Mole/25 mu l).

FIG. 10 are graphic representations illustrating that intraplantar injection of DON into the hindpaw of normal rats does not affect pressure or thermal sensitivities. DON was injected (10 mu Mole/25 mu l) on day three. Both the pressure (FIG. 10A) and thermal (FIG. 10B) sensitivities in DON-treated rats were the same as saline controls.

FIG. 11A is a graphic representation demonstrating the efficacy of N-ethylmaleimide (NEM) to provide long term pain relief to pressure (mechanical stimulation). After administration of NEM (10 mM/25 mu l) at day three following CFA inflammation, pain relief occurred for several days.

FIG. 11B is a graphic representation illustrating the efficacy of NEM to provide long term pain relief from heat. After administration of NEM (10 mM/25 mu l) at day three following CFA inflammation, pain relief occurred to near normal levels at days 4 and 6.

FIG. 12 are photomicrographs illustrating glutamate immunoreactivity in tissue sections from the hindpaw skin of a control rat (FIG. 12A), a rat after CFA inflammation (FIG. 12B), and a rat after CFA inflammation and following glutaminase inhibition with NEM (FIG. 12C).

FIG. 13A is a graphic representation demonstrating the use of two inhibitors at regulatory sites on glutaminase and their efficacy to provide long term pain relief to pressure (mechanical stimulation). After administration of Palmitoyl Coenzyme A (P-CoA, 2 mM/25 mu l) or bromothymol blue (BB, 200 mu M/25 mu l) at day three following CFA inflammation, pain relief occurred for several days.

FIG. 13B is a graphic representation illustrating the efficacy of P-CoA and BB to give long term pain relief to heat. After administration of P-CoA (2 mM/25 mu l) at day three following CFA inflammation, pain relief occurred to near normal levels from Days 4-7. After BB (200 mu M/25 mu l), pain relief occurred from Days 5-7 and at near normal levels from Days 6-7.

FIG. 14 are photomicrographs illustrating that glutaminase production in many cells is regulated by zeta-crystallin:quinone oxidoreductase (ZC).

FIGS. 14A-C illustrate that ZC levels are modified during chronic inflammation. ZC-immunoreactivity (IR) was examined in the rat L4 DRG during inflammation at an early and later time point (2, 6 days). ZC-IR in DRG neurons of control rats (A) shows a moderate staining of the cytoplasm of all neurons. Following inflammation for 48 hrs, ZC-IR is elevated in the cytoplasm and now appears in the nuclei of many neurons (arrows). ZC-IR remains elevated at 6 days of inflammation and occurs mainly in the cytoplasm although some nuclei (arrows) contain light ZC-IR.

FIG. 15 is a diagrammatic representation that illustrates that dicoumarol, a ZC inhibitor, disrupts increased glutaminase production during chronic

inflammation and decreases the prolonged hyperalgesia of chronic inflammation. Inflammation was initiated with complete Freund's adjuvant (CFA) at Day 0, and dicoumarol (15  $\mu$ l @ 500  $\mu$ M) or saline was administered intrathecally on days 0, 1 and 2. Thermal latencies and pressure responses (not shown) were recorded, and both the groups with inflammation (CFA) and inflammation plus dicoumarol (CFA+DC) experienced hyperalgesia and allodynia during acute inflammation (Day 1). As inflammation progressed, however, the responses of CFA+DC rats became less hyperalgesic and allodynic. At Day 3, the DRG's from the rats were collected and processed for glutaminase and ZC-IR, as shown in FIG. 16. FIG. 16 are photomicrographs illustrating that dicoumarol inhibits ZC and glutaminase production. In the DRG, ZC-IR was elevated (A) in rats with inflammation, but the ZC-IR (B) from rats treated with DC during inflammation was similar to controls. ZC-IR was found in the cytoplasm and nuclei (arrows) from rats with inflammation, whereas in rats treated with DC during inflammation, the nuclei (arrows) were not stained and ZC-IR was found primarily in the cytoplasm. In the DRG, glutaminase-IR was observed at moderate levels from controls (C), elevated following inflammation (D), and similar to controls in rats treated with DC during inflammation (E).

L11 ANSWER 4 OF 4 USPAT2 on STN

AN 2003:105835 USPAT2

TI Method of alleviating chronic pain via peripheral glutaminase regulation

IN Miller, Kenneth E., Sapulpa, OK, UNITED STATES

PA The Board of Regents of the University of Oklahoma, Norman, OK, UNITED STATES (U.S. corporation)

PI US 7288246 B2 20071030

AI US 2002-245098 20020913 (10)

PRAI US 2001-318861P 20010913 (60)

DT Utility

FS GRANTED

LN,CNT 1681

INCL INCLM: 424/094,100

INCLS: 514/439,000; 514/456,000; 514/558,000; 514/561,000

NCL NCLM: 424/094,100

NCLS: 514/439,000; 514/456,000; 514/558,000; 514/561,000

IC IPCI A61K0038-43 [ICM,7]; A61K0031-385 [ICS,7]; A61K0031-353 [ICS,7];

A61K0031-352 [ICS,7,C\*]; A61K0031-198 [ICS,7]; A61K0031-195

[ICS,7]; A61K0031-20 [ICS,7]; A61K0031-185 [ICS,7,C\*]

IPC1-2 A61K0038-43 [I,A]; A61K0031-385 [I,A]; A61K0031-353 [I,A];

A61K0031-352 [I,C\*]; A61K0031-198 [I,A]; A61K0031-20 [I,A];

A61K0031-185 [I,C\*]

IPCR A61K0038-43 [I,C]; A61K0038-43 [I,A]; A61K0031-00 [I,C\*];

A61K0031-00 [I,A]; A61K0031-185 [I,C]; A61K0031-198 [I,A];

A61K0031-20 [I,A]; A61K0031-35 [I,C\*]; A61K0031-35 [I,A];

A61K0031-352 [I,C]; A61K0031-353 [I,A]; A61K0031-385 [I,C];

A61K0031-385 [I,A]

EXF 424/94,1; 514/557; 514/561; 514/564; 514/570; 514/439; 514/456; 514/558

CAS INDEXING IS AVAILABLE FOR THIS PATENT.